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Frontiers in Molecular Neuroscience – résumé and perspective

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The open access journal *Frontiers in Molecular Neuroscience* has existed since 2008. Publications started with an inaugural Research Topic centered on molecular mechanisms of the regulation of excitatory and inhibitory synapses in the brain – also known as E–I balance. This topic addressed the necessity of excitation and inhibition for cognitive function and how both types of transmission need to be co-regulated in order to avoid synaptic dysfunction. De-regulation of the E–I balance is associated with a number of neurological disorders including epilepsy and intellectual disability (Eichler and Meier, 2008; Fritschy, 2008; Harvey et al., 2008; Kehrer et al., 2008). Hence, an understanding of regulatory mechanisms at systemic, network, cellular, and molecular levels is a prerequisite for the development of novel and effective pharmacological therapies. However, we still need to learn and understand how the highly interconnected signaling networks function on a temporal basis, which is required to orchestrate proper brain function. Thus, it is also important to understand synaptic transmission at the level of individual receptors, such as $GABA_A$, glycine, and glutamate receptors (Keith and El-Husseini, 2008; Tretter and Moss, 2008). In addition to synaptic mechanisms, the role of non-synaptic neurotransmitter receptor signaling can also play a fundamental role (Stell and Mody, 2002; Sierra-Paredes and Sierra-Marcuno, 2007; Zhang et al., 2007; Muller et al., 2008; Legendre et al., 2009).

In order to understand how disease-related changes in molecular and cellular mechanisms impact on cognitive processing and brain function in general, it is important to invent experimental tools for targeted manipulation of neuronal activity. In this context, papers focusing on advanced techniques for visualization and manipulation of neuronal activity have helped address unmet needs, placing the journal at the cutting edge of this molecular revolution (Wisden and Meier, 2010). In particular, cell type-selective manipulations of neuronal activity can be achieved with light (Alilain and Silver, 2009; Han et al., 2009; Adamantidis et al., 2010), ligand–receptor combinations (Nichols and Roth, 2009; Wisden et al., 2009), K^+ channels (Hodge, 2009), and tethered toxins (Holford et al., 2009). Gene targeting and virally mediated gene expression in mice continues to yield gains (Heldt and Ressler, 2009; Reijmers and Mayford, 2009; Weber et al., 2009). Moreover, model organisms such as *Drosophila* and zebrafish are increasingly valuable, as they allow rapid generation of transgenic animals or targeted knockdowns and investigation of the systemic changes that result from targeted manipulation of neuronal activity (Kasuya et al., 2009; Tessier and Broadie, 2009; White and Peabody, 2009; Hirata et al., 2010). Molecular systems for monitoring ion flux across the neuronal plasma membrane as well as high-throughput drug screening approaches will also help to develop novel pharmacological tools for treating neurological disorders (Bregestovski et al., 2009; Gilbert et al., 2009; Perron et al., 2009).

Advanced sequencing technologies will play an increasing role in neuroscience, providing us with important information about exomic, genomic, and RNA splice variants. Epigenetic modulation via genomic DNA methylation, regulating gene transcription, is also a rapidly emerging field (Eid et al., 2009; Li et al., 2009; Flusberg et al., 2010). However, it is important to determine whether these polymorphisms, variants, and modifications are relevant to disease. Thus, functional studies that link DNA/RNA polymorphisms or DNA methylation to specific disease states will be required for years to come. A holistic approach involving genomics, RNomics, and proteomics in combination with bioinformatics and computational neuroscience will help create corresponding databases and constitute the basis for multimodal and interdisciplinary views of disease mechanisms. Understanding these multimodal relationships via a multidisciplinary approach should be our primary goal (Engmann and Giese, 2009; Harvey et al., 2009; Legendre et al., 2009; Liebl et al., 2009; Phuket and Covarrubias, 2009; Rivera-Arconada et al., 2009; Poulter et al., 2010).

In summary, the first 3 years of *Frontiers in Molecular Neuroscience* have been a resounding success, with over 100 articles and 18 Research Topics published to date. The long-term goal of *Frontiers in Molecular Neuroscience* is to continue publishing the latest findings and conceptual advances in neurobiology (see for example Albrecht, 2011; Carulli et al., 2011; Hideyama and Kwak, 2011; Kaidanovich-Beilin and Woodgett, 2011; Li et al., 2011; Tonges et al., 2011; Weiss, 2011; Zhang et al., 2011). We therefore encourage researchers to submit novel and stimulating findings to *Frontiers in Molecular Neuroscience* in 2012 and warmly thank all authors and editors for their invaluable support of *Frontiers in Molecular Neuroscience*.

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